REMARKS/ARGUMENTS

I. Status of the claims

Claim 28 is amended. Claims 28-33 and 40-50 are pending, and claims 1-27, 34-39, and 51-56 are withdrawn.

II. Restriction

Applicants understand that the Examiner has maintained the restriction. Nevertheless, Applicants request that the Examiner reconsider the restriction with regard to SEQ ID NO:74 and the presently examined sequences because SEQ ID NO:9 (currently under examination) and SEQ ID NO:74 are identical. As the two sequences are identical, Applicants respectfully request that the Examiner reconsider examination of claims 37-39 with the claims currently under examination.

III. Support for the Amendments

Support for the amendments can be found throughout the specification and claims as originally filed. For example, support for the amendments to claim 28 can be found in the originally filed claim. The original claim recited a second oligonucleotide that hybridized to SEQ ID NO:9 or a complement thereof. As amended, the claim is directed to an oligonucleotide that hybridizes to the complement of SEQ ID NO:9. Accordingly, no new matter is added.

IV. Obviousness Rejection

1. Introduction

The Examiner rejected various claims under 35 U.S.C. § 103 as allegedly obvious. In particular, the Examiner rejected claims 28, 40, 41, and 48-50 over Erlich et al. (U.S. Pat. No. 6,040,166 in view of Beasley et al. and Lanciotti et al (2002) with Buck et al. in support, claims 29-33 over Erlich et al. in view of Beasley et al. and Lanciotti et al (2002) with Buck et al. in support in view of Will (U.S. Pat. No. 6001611), claims 42 and 47 over Erlich et al. in view of Beasley et al. and Lanciotti et al (2002) with Buck et al. in support in view of

Rigler et al. (1998), and claim 44 over Erlich et al. in view of Beasley et al. and Lanciotti et al (2002) with Buck et al. in support in view of Lanciotti et al (2001). Applicants respectfully traverse the rejections.

The Examiner argues that:

(1) the Elrich reference describes kits for detection and amplification of nucleic acids;

(2) the Beasley reference allegedly describes "a sequence comprising SEQ ID NO:8 for flavivirus West Nile" (Final Office Action, page 5);

the Lanciotti reference describes "genomic West Nile virus ... corresponding to SEQ ID NOs:9 and 16" (Final Office Action, page 5).

In view of the above art, the Examiner argued that the recited primers and probes were *prima facie* "obvious for representing structural homologs of the genomic flavivirus nucleotides." The Examiner further argued that there was a reasonable expectation of success using any potential primer sequences in view of the Buck reference.

2. Legal Standard

The Examiner has not set forth a *prima facie* case of obviousness. A proper *prima facie* case of obviousness requires that the Examiner establish: 1) that the elements of the claimed invention are in the prior art, 2) that there is a motivation to combine the elements as claimed, and 3) that there is an objective reason why those of skill in the art would have had a reasonable expectation that the combined elements function as intended. *See* MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

An applicant can overcome a rejection by showing insufficient evidence of *prima facie* obviousness or by rebutting the *prima facie* case with evidence of secondary indicia of nonobviousness. Secondary indicia of nonobviousness include unexpected results created by the claimed invention and/or unexpected properties of the claimed invention.

3. Summary Of Arguments

In the present case, the Examiner has not shown there is an objective reason why those of skill in the art would have had a reasonable expectation that the claimed kit components would function as intended. The Examiner relies on two *different* viral genome sequences to argue that generation of the claimed kit is obvious. However, one of ordinary skill does not generally design primer combinations in this way. Further, certain prior art taught away from design of single detection assays that detected more than one viral species. Thus the Examine has not set forth a *prima facie* obviousness rejection.

In addition, the claimed kit has unexpected and surprising properties. For example, it was not predictable, and therefore it was surprising that, the claimed primer/probe set was capable of detecting a wide range of different flaviviruses (e.g., West Nile Virus (WNV), St. Louis encephalitis virus (SLEV), Murray Valley encephalitis virus and Japanese encephalitis virus (JEV) (*see, e.g.*, the specification at paragraph 6, lines 21-23), rather than *only* WNV. Further, it is particularly surprising that the claimed kit can detect SLEV because the 3' sequences of SLEV (corresponding to SEQ ID NO:9) were not known as of the filing date of the present application. Finally,

4. The Examiner Has Not Set Forth A *Prima Facie* Rejection

a. There Is No Reasonable Expectation Of Success When Two Different Genomes Are Used As The Basis For A Proposed Amplification Scheme

There was no reasonable expectation of success for designing primers from two different viral sequences that amplify a particular viral sequence. The Examiner argues that it would be obvious to design a kit for amplifying West Nile Virus (WNV) based on the specific sequences identified in the Examiner sequence searches for SEQ ID NO: 8 and SEQ ID NO:9. Specifically, the Examiner noted that Beaseley *et al.* allegedly describes a sequence comprising SEQ ID NO:8, whereas Lanciotti *et al.* allegedly describes a sequence comprising SEQ ID NO:9.

The Examiner relies on the Buck reference to argue that essentially any primer set designed from a *particular* sequence will be effective to amplify the *particular* sequence.

However, those are not the facts the Examiner presents in the obviousness rejection. Instead, the rejection is based on the alleged obviousness of designing one primer for one viral isolate (the one allegedly described by Beasley *et al.*) and a second primer as well as a probe for another viral isolate (the one allegedly describe by Lanciotti *et al.*). While it may be possible to design primers that hybridize to the respective sequences, it would not at all be clear to one of ordinary skill in the art which of the two sequences, if any, would be amplified using the so-designed primers and probes because, as set forth by the Examiner, the primers were not both designed from a single target sequence. Accordingly, the Examiner has not established that there was a reasonable expectation of success for using the recited oligonucleotides to amplify any particular sequence.

b. Various Lanciotti References Taught Away From Design Of Primers That Amplify Non-WNV Viruses

The recited kit is capable of amplifying a variety of flavivirus species, including West Nile Virus (WNV), Japanese encephalitis virus (JEV), Dengue virus and St. Louise encephalitis virus (SLEV). In contrast, certain prior art taught away from designing primers capable of amplifying various different flaviviruses. Thus, it was not obvious to design the particular recited kit of oligonucleotides because the cited art taught away from their design.

Lanciotti, *et al.*, *J. Clin. Microbiol.* 38(11):4066-4071 (attached as Exhibit A) describes the rapid detection of WNV using a TaqMan assay. Notably, the paper emphasizes the "specific" nature of the assay (e.g., on page 4066, right column). The specificity of the assay for West Nile Virus strains was also described and emphasized in the sentence spanning pages 4069-70, saying in part "no false-positive results were obtained with any of the serologically related flaviviruses tested or with any of the other domestic arthropod-borne viruses tested."

In another Lanciotti paper (*J. Clin. Microbiol.* 39(12):4506-4513 (2001))(attached as Exhibit B), the author describes assays for detecting WNV and SLEV. However, instead of designing one assay to detect both viruses, the authors designed two different assays, each *specific* for one type of virus (WNV and SLEV, respectively).

Accordingly, the art described design of detection assays that detected specific viral species (e.g., WNV *or* SLEV, etc.) ***only*** and accordingly taught ***away*** from design of a single assay to detect multiple flaviviruses.

5. The Claimed Invention Has Surprising Properties

a. It Is Surprising That The Kit Is Capable Of Detecting Viruses Other Than WNV Within The Japanese Encephalitis Serogroup

Assuming *arguendo* a *prima facie* case of obviousness has been made, objective indicia of non-obviousness successfully rebuts the *prima facie* showing. *See, Rosemount, Inc., v. Beckman Instruments, Inc.,* 221 USPQ 1 (Fed. Cir. 1984); *Dow Chemical co. v. American Cyanamid Co.,* 2 USPQ2d 1350 (Fed. Cir. 1987). Objective evidence of non-obviousness include unexpected results created by the claimed invention and/or unexpected properties of the claimed invention

As described in the present application (e.g., paragraph 6, lines 21-23), the claimed kit is capable of detecting a number of different viruses, including West Nile Virus (WNV), St. Louis encephalitis virus (SLEV), Murray Valley encephalitis virus (MVEV) and Japanese encephalitis virus (JEV). Even if the Examiner has set forth a *prima facie* obviousness rejection (which Applicant disputes), there was no reasonable expectation that the kit would also be able to detect SLEV, MVEV, and JEV. Indeed, it is a surprising result that not only are the kit components useful to detect a specific strain of WNV but that they are broadly useful for detection of a number of different viruses.

It is particularly surprising that the claimed oligonucleotides are capable of amplification of SLEV or MVEV given the differences in the genomic sequences of viruses compared to the claimed oligonucleotides. This is illustrated, for example, in Figure 1, which shows SEQ ID NO:8 at the top of the Figure and SLEV and MVEV genomic sequences on the fourth page of Figure 1. The fourth page of Figure 1 shows that SEQ ID NO:8 is not completely complementary to the SLEV and MVEV genomes and yet SEQ ID NO:8 is still effective in combination with the other recited oligonucleotides to amplify and detect SLEV and MVEV.

This represents a surprising result given the differences between the primer and SLEV/MVEV genomes.

b. The Ability Of The Recited Sequences To Amplify SLEV Was Surprising As The Nucleotide Sequence Of The SLEV Genome Corresponding To SEQ ID NO:9 Was Not Known As Of The Priority Date

At the time the patent application was filed, it was particularly surprising that the oligonucleotides recited in the present claims could detect St. Louis encephalitis (SLEV). *See, e.g.*, the present specification, paragraph 6, lines 21-23. This represents a surprising aspect of the claimed invention because the 3' sequence of the SLEV genome, including the portion of the genome corresponding to SEQ ID NO:9, was ***not known*** as of the priority date of the present application. Thus, it would have been impossible for one of skill in the art to predict that the claimed kit would be capable of detecting SLEV. Accordingly, to the extent the Examiner has presented a *prima facie* obviousness rejection (which Applicant disputes), the ability of the recited kit to detect SLEV rebuts the rejection.

6. Summary

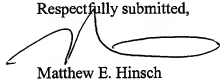
As discussed above, the present claims are not obvious in view of the cited art. Accordingly, withdrawal of the rejections is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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